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  * * * * * * * * * * * * * STN  Columbus  * * * * * * * * * * * * * *

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=> index biosci
FILE 'DRUGMONOG' ACCESS NOT AUTHORIZED
COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                       ENTRY    SESSION
FULL ESTIMATED COST                                     0.21       0.21

INDEX 'ADISCTI, ADISINSIGHT, ADISNEWS, AGRICOLA, ANABSTR, AQUASCI, BIOBUSINESS,
       BIOCOMMERCE, BIOSIS, BIOTECHABS, BIOTECHDS, BIOTECHNO, CABA, CANCERLIT,
       CAPLUS, CEABA-VTB, CEN, CIN, CONFSCI, CROPB, CROPU, DISSABS, DDFB, DDFU,
       DGENE, DRUGB, DRUGMONOG2, ...' ENTERED AT 14:08:53 ON 12 APR 2004

68 FILES IN THE FILE LIST IN STNINDEX

Enter SET DETAIL ON to see search term postings or to view
search error messages that display as 0* with SET DETAIL OFF.

=> s aprotinin (p) (t-PA or tissue (w) plasminogen (w) activator) (p)
composition
          0*  FILE ADISNEWS
          0*  FILE BIOCOMMERCE
          3*  FILE BIOTECHABS
          3*  FILE BIOTECHDS
          1*  FILE BIOTECHNO
          0*  FILE CEABA-VTB
          0*  FILE CIN
  21 FILES SEARCHED...
          1   FILE DRUGU
          1   FILE EMBAL
          1   FILE EMBASE
          1*  FILE ESBIOBASE
  33 FILES SEARCHED...
          0*  FILE FEDRIP
          0*  FILE FOMAD
          0*  FILE FOREGE
          0*  FILE FROSTI
          0*  FILE FSTA
          5   FILE IFIPAT
          0*  FILE KOSMET
          0*  FILE MEDICONF
          1   FILE MEDLINE
          0*  FILE NTIS
          0*  FILE NUTRACEUT
          0*  FILE PASCAL
  52 FILES SEARCHED...
          0*  FILE PHARMAML
          1   FILE SCISEARCH
          1   FILE USPATFULL
          2   FILE WPIDS
          2   FILE WPINDEX

  13 FILES HAVE ONE OR MORE ANSWERS,   68 FILES SEARCHED IN STNINDEX

L1   QUE APROTININ (P) (T-PA OR TISSUE (W) PLASMINOGEN (W) ACTIVATOR) (P) COMPO
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COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                       ENTRY    SESSION
FULL ESTIMATED COST                                     1.71       1.92

FILE 'IFIPAT' ENTERED AT 14:10:53 ON 12 APR 2004
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<------User Break------>

SEARCH ENDED BY USER

=> s l1
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FIELD CODE - 'AND' OPERATOR ASSUMED 'APROTININ (P) '
PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH
FIELD CODE - 'AND' OPERATOR ASSUMED 'CTIVATOR) (P) COMPOSITI'
PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH
FIELD CODE - 'AND' OPERATOR ASSUMED 'APROTININ (P) '
PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH
FIELD CODE - 'AND' OPERATOR ASSUMED 'CTIVATOR) (P) COMPOSITI'
PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH
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FIELD CODE - 'AND' OPERATOR ASSUMED 'APROTININ (P) '
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FIELD CODE - 'AND' OPERATOR ASSUMED 'CTIVATOR) (P) COMPOSITI'
L2          18 L1

=> dup rem l2
PROCESSING COMPLETED FOR L2
L3           14 DUP REM L2 (4 DUPLICATES REMOVED)

=> d l3 trial 1-14

L3   ANSWER 1 OF 14  IFIPAT  COPYRIGHT 2004 IFI on STN
AN    04009634  IFIPAT;IFIUDB;IFICDB
TI    TISSUE INHIBITOR OF METALLOPROTEINASE TYPE THREE (TIMP-3) COMPOSITION AND
      METHODS
CLMN  17
NCL   NCLM: 530350000
      NCLS: 435226000; 514012000; 530300000
      [07]
IC    ICM: C07K001-00
      ICS: C07K014-00; C12N009-64

L3   ANSWER 2 OF 14  EMBAL COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED. on
     STN                                          DUPLICATE 1
TI   Plasma MMP-2 and MMP-9 and their inhibitors TIMP-1 and TIMP-2 during human
     orthotopic liver transplantation. The effect of aprotinin and the relation
     to ischemia/reperfusion injury.
ST   Aprotinin; Ischemia/reperfusion injury; Liver transplantation; Matrix
     metalloproteinases; Plasmin

L3   ANSWER 3 OF 14  IFIPAT  COPYRIGHT 2004 IFI on STN DUPLICATE 2
AN    10381108  IFIPAT;IFIUDB;IFICDB
TI    PROCESS FOR PREPARING SCHIFF BASE ADDUCTS OF AMINES WITH O-HYDROXY
      ALDEHYDES AND COMPOSITIONS OF MATTER BASED THEREON
CLMN  28
NCL   NCLM: 530409000
      NCLS: 530410000
      [07]
IC    ICM: C07K014-00

L3   ANSWER 4 OF 14  IFIPAT  COPYRIGHT 2004 IFI on STN
AN    10188232  IFIPAT;IFIUDB;IFICDB
TI    BIOPOLYMER MEMBRANE AND METHODS FOR ITS PREPARATION; STRUCTURE HAVING
      HETATIC, NON- ADHESIVE, AND ANTI-ADHESION PROPERTIES; ARTIFICIAL SKINS
CLMN  72
NCL   NCLM: 424001110
      NCLS: 424094640; 424130100; 424443000; 514002000; 514054000
      [07]
IC    ICM: A61K051-00
      ICS: A61K009-70; A61K031-715; A61K038-48; A61K039-395

L3   ANSWER 5 OF 14  IFIPAT  COPYRIGHT 2004 IFI on STN
AN    03661662  IFIPAT;IFIUDB;IFICDB
TI    HYDROPHOBIC PREPARATIONS OF HYDROPHILIC SPECIES AND PROCESS FOR THEIR
      PREPARATION; ANHYDROUS; OPTICAL CLARITY; MACROMOLECULES
CLMN  20
NCL   NCLM: 424450000
      NCLS: 264004100; 264004300; 424094300; 424812000; 514002000; 514003000;
          514006000; 514008000; 514021000; 514044000; 514937000
      [07]
IC    ICM: A61K009-127
      ICS: A61K038-00; A61K009-133

L3   ANSWER 6 OF 14  BIOTECHDS COPYRIGHT 2004 THOMSON DERWENT/ISI on STN
AN   2003-02750  BIOTECHDS
TI   Novel synthetic fibrin-binding moiety, useful for detecting, imaging or
     localizing fibrin-containing clots by magnetic resonance imaging,
     radioimaging and for treating diseases involving thrombus formation e.g.
     stroke;
        fibrin-binding protein preparation by solid phase peptide synthesis
        for disease therapy
CC   THERAPEUTICS, Protein Therapeutics; GENETIC TECHNIQUES and APPLICATIONS,
     Gene Expression Techniques and Analysis; DISEASE, Cancer; DISEASE,
     Cardiovascular; DISEASE, Endocrine/Metabolic System; DISEASE, Respiratory
     System; DISEASE, Liver; DISEASE, Kidney; DISEASE, Autoimmune Disease;
     DISEASE, Other Diseases; DIAGNOSTICS, Molecular Diagnostics
CT   RECOMBINANT FIBRIN-BINDING PROTEIN PREP., RECOMBINANT PHAGE-MEDIATED GENE
     TRANSFER, EXPRESSION IN HOST CELL, SOLID PHASE PEPTIDE SYNTH.,
     FLUORESCENT, ECHOGENIC, RADIOACTIVE, PARAMAGNETIC LABEL, CHELATOR,
     MAGNETIC RESONANCE IMAGING, ELISA, PHAGE LIBRARY, DNA SEQUENCING, APPL.
     DEEP-VEIN THROMBOSIS, LUNG EMBOLISM, CARDIOGENIC THROMBOSIS,
     ATHEROSCLEROSIS, STROKE, HEART, KIDNEY, LIVER, LUNG, BRAIN HYPOXIA,
     ISCHEMIA, CANCER, DIABETIC RETINOPATHY, ATHEROSCLEROSIS, AUTOIMMUNE
     DISEASE, INFLAMMATORY DISORDER THERAPY, DIAGNOSIS, DRUG SCREENING
     FLUORESCENCE ANALYSIS IMMUNOASSAY TUMOR DNA SEQUENCE PROTEIN SEQUENCE
     (22, 05)|

L3   ANSWER 7 OF 14  BIOTECHDS COPYRIGHT 2004 THOMSON DERWENT/ISI on STN
AN   2002-18792  BIOTECHDS
TI   Compound which inhibits binding of  ***tissue***  ***plasminogen***
       ***activator***  to endothelial cells, useful for stimulating
     proliferation of endothelial cells and in wound healing, coronary artery
     disease and critical limb ischemia;
        recombinant protein production, drug screening and antibody useful for
        gene therapy
CC   THERAPEUTICS, Protein Therapeutics; GENETIC TECHNIQUES and APPLICATIONS,
     Gene Expression Techniques and Analysis; PHARMACEUTICALS, Antibodies;
     DISEASE, Cancer; DISEASE, Autoimmune Disease; DISEASE,
     Endocrine/Metabolic System; DISEASE, Cardiovascular; DISEASE, Other
     Diseases; THERAPEUTICS, Gene Therapy
CT   RECOMBINANT KRINGLE-2 PROTEIN PREP., VECTOR-MEDIATED GENE TRANSFER,
     EXPRESSION IN HOST CELL,  ***TISSUE***  ***PLASMINOGEN***  -
       ***ACTIVATOR***  , ENDOTHELIAL CELL BINDING INHIBITION, MONOCLONAL
     ANTIBODY, DRUG SCREENING, APPL. VULNERARY, CORONARY ARTERY DISEASE,
     CRITICAL LIMB ISCHEMIA, TUMOR, RHEUMATOID ARTHRITIS, DIABETIC RETINOPATHY
     THERAPY, GENE THERAPY DNA SEQUENCE PROTEIN SEQUENCE CYTOSTATIC
     ANTIRHEUMATIC ANTIDIABETIC VASOTROPIC CARDIANT  (21, 50)|

L3   ANSWER 8 OF 14  WPIDS  COPYRIGHT 2004 THOMSON DERWENT on STN
AN   2001-182932 [18]   WPIDS
DNC  C2001-054613
TI   Novel amide of bile salt which is conjugated to a biologically active
     substance useful for improving and/or increasing bioavailability of
     biologically active substance when administered orally or parenterally.
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DC B04
IC ICM C07J000-00; C07K014-595; C07K017-00
ICS A61K038-04; A61K047-28; A61K047-48; C07K014-47; C07K014-575
MC CPI: B01-D02; B04-B04H; B04-C01A; B04-C01G; B04-C02; B04-E01; B04-G01; B04-H06; B04-H07; B04-J01; B04-L01
PNC 4
CYC 95

L3 ANSWER 9 OF 14 WPIDS COPYRIGHT 2004 THOMSON DERWENT on STN
AN 2000-376312 [32] WPIDS
DNC C2000-113747
TI Composition for treating blood coagulation disorders, particularly deficiency of von Willebrand factor, containing a receptor-binding competitor to extend protein half-life.
DC B04 D16
IC ICM A61K038-36; A61K038-37
ICS A61K038-16; A61K038-43; A61K038-46; A61K038-48; A61K047-42; A61P007-04; C07K014-745; C07K014-755; C07K014-81
ICI A61K038:16; A61K038-37, A61K038:17, A61K038:40, A61K038:49, A61K038:57; A61K038:57; A61K038:49; A61K038:40; A61K038:17; A61K038:16; A61K038-37
MC CPI: B04-C01; B04-H19; B04-N04; B14-F08; D05-C12; D05-H13; D05-H17
PNC 6
CYC 91

L3 ANSWER 10 OF 14 Elsevier BIOBASE COPYRIGHT 2004 Elsevier Science B.V. on STN
AN 1998273360 ESBIOBASE
TI Platelets and soluble fibrin promote plasminogen activation causing downregulation of platelet glycoprotein Ib/IX complexes: Protection by ***aprotinin***
CC 82.12.2.3 PROTEIN BIOCHEMISTRY: OTHER PROTEINS: Non-Haem Blood Proteins: Platelet proteins
89.1.1.3 CELL AND DEVELOPMENTAL BIOLOGY: MEMBRANES AND CELL TRANSPORT: Cell Surface and Plasma Membrane: Proteins and glycoproteins
89.4.1.1 CELL AND DEVELOPMENTAL BIOLOGY: EXTRACELLULAR MATRIX (STRUCTURE AND FUNCTION): Extracellular Matrix: Structure and ***composition***
89.5.1.2 CELL AND DEVELOPMENTAL BIOLOGY: CELL TYPES AND BIOLOGY: Cell Types: Blood cells
ST Platelets; Soluble fibrin; Fibrinolysis; Glycoprotein Ib/IX; Hemostasis; Cardiopulmonary bypass

L3 ANSWER 11 OF 14 BIOTECHNO COPYRIGHT 2004 Elsevier Science B.V. on STN
AN 1995:25266927 BIOTECHNO
TI Fibrinolysis inhibits shear stress-induced platelet aggregation
CT *alteplase; * ***tissue*** ***plasminogen*** ***activator*** ; *coronary artery thrombosis; *fibrinolysis; fibrinogen receptor; ***aprotinin*** ; glycoprotein ib; glycoprotein iib; glycoprotein iiia; plasmin; prostacyclin; von willebrand factor; article; controlled study; coronary artery blood flow; dose response; drug mechanism; human; human cell; plasminogen activation; priority journal; shear stress; thrombocyte aggregation

L3 ANSWER 12 OF 14 IFIPAT COPYRIGHT 2004 IFI on STN
AN 02354886 IFIPAT;IFIUDB;IFICDB
TI ORAL COMPOSITIONS OF PROTEINACEOUS MEDICAMENTS; PROTEASE INHIBITOR; PHOSPHOLIPID; CHOLESTEROL; SURFACTANT; ERYTHROPOIETIN, INSULIN; LIQUID LIPID SOLVENT
CLMN 13
NCL NCLM: 514003000
NCLS: 424455000; 424463000; 424474000; 424490000
IC ICM: A61K009-10
ICS: A61K037-02; A61K009-48; A61K009-66

L3 ANSWER 13 OF 14 BIOTECHDS COPYRIGHT 2004 THOMSON DERWENT/ISI on STN
AN 1989-10956 BIOTECHDS
TI Effect of harvest medium ***composition*** on yield and chain nature of recombinant tissue-type plasminogen-activator species; produced by mouse recombinant C127 fibroblast cell line TRC 310 or TRC 320/8
CC J CELL CULTURE; J1 Animal Cell Culture; D PHARMACEUTICALS; D5 Other Pharmaceuticals; A MICROBIOLOGY; A1 Genetics
CT RECOMBINANT ***TISSUE*** ***PLASMINOGEN*** - ***ACTIVATOR*** PREP., C127 CELL CULTURE, HARVEST CULTURE MEDIUM, PROTEIN HYDROLYZATE EFFECT ON YIELD, ETC. THROMBOLYTIC ENZYME PROTEASE MOUSE MAMMAL FIBROBLAST|

L3 ANSWER 14 OF 14 DRUGU COPYRIGHT 2004 THOMSON DERWENT on STN
AN 1987-31980 DRUGU P
TI Evidence for the Progressive Uptake of APSAC by Human Clots In Vitro.
CC 18 Hematological
73 Trial Preparations
CT NORLEUCINE *RC; FIBRIN *RC; PLASMINOGEN *RC; IN-VITRO *FT; HUMAN *FT; THROMBUS *FT; THROMBOSIS *FT; IODINE-LABELED *FT; THROMBOLYTIC *FT; BLOOD-PLASMA *FT; BINDING *FT; BLOOD-CLOTTING-FACTOR *FT
[01] BRL-26921 *PH; THROMBOLYTICS *FT; ENZYMES *FT; EC-0.0.0.0 *FT; TRIAL-PREP. *FT; BRL-26921 *RN; PH *FT
[02] UROKINASE *PH; THROMBOLYTICS *FT; ENZYMES *FT; EC-3.4.21.31 *FT; UROKINASE *RN; PH *FT
[03] STREPTOKINASE *PH; THROMBOLYTICS *FT; ENZYMES *FT; EC-0.0.0.0 *FT; STREPTOKI *RN; PH *FT

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COST IN U.S. DOLLARS SINCE FILE ENTRY 16.39 TOTAL SESSION 18.31
FULL ESTIMATED COST

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COST IN U.S. DOLLARS SINCE FILE ENTRY 0.63 TOTAL SESSION 18.94
FULL ESTIMATED COST

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=> d l3 7, 9, 11 bib ab

L3 ANSWER 7 OF 14 BIOTECHDS COPYRIGHT 2004 THOMSON DERWENT/ISI on STN
AN 2002-18792 BIOTECHDS
TI Compound which inhibits binding of ***tissue*** ***plasminogen*** ***activator*** to endothelial cells, useful for stimulating proliferation of endothelial cells and in wound healing, coronary artery disease and critical limb ischemia;
recombinant protein production, drug screening and antibody useful for gene therapy
AU CARROLL V; HARRIS A; BICKNELL R; PRICE P
PA ISIS INNOVATION LTD
PI WO 2002043747 6 Jun 2002
AI WO 2000-GB5244 28 Nov 2000
PRAI GB 2000-29001 28 Nov 2000
DT Patent
LA English
OS WPI: 2002-508478 [54]
AB DERWENT ABSTRACT:
NOVELTY - A compound (I) which inhibits binding of ***tissue*** ***plasminogen*** ***activator*** (tPA) to endothelial cells useful for stimulating proliferation of endothelial cells, is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following: (1) a kringle 2 domain (II) of tPA or its variant for reducing endothelial cell proliferation or inducing cell death; (2) a combination (III) of (I) and a tPA or its fragment comprising the finger domain or its variant for simultaneous or sequential administration for stimulating proliferation of endothelial cells; (3) a combination (IV) of (I) and a compound which inhibits binding of the finger domain of tPA to endothelial cells, for simultaneous or sequential administration for reducing endothelial cell proliferation or inducing cell death; (4) a polynucleotide (V) encoding (II) and comprising a 246 base pair sequence, given in the specification, or its variant for reducing endothelial cell proliferation or inducing cell death; and (5) an expression vector (VI) comprising (V).

WIDER DISCLOSURE - (1) polynucleotide comprising a contiguous sequence of nucleotides that hybridizes to the coding sequence or complement of coding sequence of 527 amino acids defined in the specification, and to (S1); (2) antibodies specific for (II), useful for detecting (II); and (3) ***composition*** for stimulating proliferation of endothelial cells by modulating the effect of (II) on endothelial cells.

BIOTECHNOLOGY - Preferred Compound: (I) comprises an anti-kringle 2 domain antibody.

ACTIVITY - Anti-tumor; Antirheumatic; Antiarthritic; Antidiabetic; Vulnerary; Vasotropic; Cardiant.

MECHANISM OF ACTION - Inhibitor of binding of (II) to endothelial cells; modulator of cell growth; gene therapy. No biological data is given.

USE - (I) is useful for stimulating proliferation of endothelial cells. The method comprises contacting the cells with (I) and further with tPA or its fragment comprising finger domain of tPA or its variant. (I) and (III) are useful in wound healing, coronary artery disease and critical limb ischemia. (II) is useful for identifying a substance which stimulates proliferation of endothelial cells, by incubating (II) with an endothelial cell membrane in the presence of a test substance, monitoring for binding of the kringle 2 domain to the endothelial cell membrane, and determining whether the test substance is useful in stimulating proliferation of endothelial cells, and further formulating the test substance identified as stimulating proliferation of endothelial cells with a carrier. (II) and (IV) are useful for reducing endothelial cell proliferation or inducing cell death. (II), (IV), (V) and (VI) are useful for treating solid tumors, rheumatoid arthritis and diabetic retinopathy. (All claimed). (V) is useful in recombinant protein synthesis and as therapeutic agents used in gene therapy techniques.

ADMINISTRATION - The inhibitor of (II) is administered at a dose of 0.1-50 mg/kg, preferably 5 mg/kg-2 g/kg, and the nucleic acid at a dose of 1 pg-1 mg, preferably 10 micro-g-1 g, by enteral, topical, oral, buccal, anal, pulmonary, intravenous, intraarterial, intramuscular or intraperitoneal route.

EXAMPLE - The effect of anti-kringle 2 antibody on endothelial cell (EC) proliferation was determined. Human umbilical vein endothelial cell (HUVEC) were incubated with a panel of monoclonal antibodies directed against the individual domains of ***tissue*** ***plasminogen*** ***activator*** (tPA) in the presence of 2 % fetal bovine serum (FBS), but no other EC growth factors. An antibody that recognized the kringle 2 (K2) domain of tPA (7VPA) caused a dose dependent increase in EC proliferation which was determined colorimetrically. A 4-fold increase in HUVEC growth was observed at 500 microg/ml, the highest concentration of antibody used which was statistically significant as compared with the lowest concentration of antibody used. Similar results were obtained when cell numbers were counted directly after adding 7VPA to HUVEC. Antibodies directed to the finger/epidermal growth factor (EGF)-like, kringle 1 (K1) or the protease domains of tPA did not have similar effects on HUVEC growth. Anti-K2 induced HUVEC proliferation was specific for EC cultures as no effect of the antibody was observed on human vascular smooth muscle cells (HVSMC) even though these cells also secrete endogenous tPA. HUVEC cultures were stimulated to proliferate with anti-K2 antibody with the simultaneous addition of antibodies directed to finger/EGF-like, kringle 1 or protease domains of tPA. An anti-finger/EGF monoclonal antibody dose-dependently inhibited HUVEC proliferation induced by anti-K2 antibody. Neither an anti-K1 antibody nor an antibody that inhibited the catalytic activity of tPA blocked the increase in cell growth. In addition, the plasmid inhibitor, ***aprotinin*** blocked anti-kringle 2 induced EC proliferation. These data suggested that binding K2, tPA mediated EC growth was not dependent on plasmin generation, but on a region of tPA located within the finger or EGF-like domains.(48 pages)

L3 ANSWER 9 OF 14 WPIDS COPYRIGHT 2004 THOMSON DERWENT on STN
AN 2000-376312 [32] WPIDS
DNC C2000-113747

TI Composition for treating blood coagulation disorders, particularly deficiency of von Willebrand factor, containing a receptor-binding competitor to extend protein half-life.
DC B04 D16
IN BINDER, B; SCHWARZ, H; TURECEK, P
PA (IMMO) IMMUNO AG; (BAXT) BAXTER AG
CYC 91
PI WO 2000027425 A2 20000518 (200032)* DE 19p
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SL SZ TZ UG ZW
W: AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ DE DK DM EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW
AU 2000012527 A 20000529 (200041)
EP 1128841 A2 20010905 (200151) DE
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI
AT 9801873 A 20011215 (200208)
AT 409335 B 20020615 (200248)
JP 2002529424 W 20020910 (200274) 27p
ADT WO 2000027425 A2 WO 1999-AT271 19991110; AU 2000012527 A AU 2000-12527 19991110; EP 1128841 A2 EP 1999-955585 19991110, WO 1999-AT271 19991110; AT 9801873 A AT 1998-1873 19981110; AT 409335 B AT 1998-1873 19981110; JP 2002529424 W WO 1999-AT271 19991110, JP 2000-580654 19991110
FDT AU 2000012527 A Based on WO 2000027425; EP 1128841 A2 Based on WO 2000027425; AT 409335 B Previous Publ. AT 9801873; JP 2002529424 W Based on WO 2000027425
PRAI AT 1998-1873 19981110
AB WO 200027425 A UPAB: 20001128
NOVELTY - Pharmaceutical ***composition*** (A) for treating disorders of blood coagulation comprises:
(i) at least one pro-protein (I) of coagulation; and
(ii) a receptor-binding competitor (II) that does not affect the physiology of coagulation.
DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:
(1) combined preparation (B) of ***aprotinin*** and ***tissue*** ***plasminogen*** ***activator*** (tPA); and
(2) use of an LRP-ligand (III) (LRP = lipoprotein receptor-related protein) for:
(i) treatment of phenotypic coagulation factor deficiency; or
(ii) increasing the biological half-life of a protein.
ACTIVITY - Antihemophilic; procoagulant.
MECHANISM OF ACTION - (II) is an in vivo stabilizer of (I) since it blocks the receptor involved in clearance and internalization of (I).
USE - (A), also compositions containing only an LRP-ligand (LRP = lipoprotein receptor-related protein), are used:
(i) to treat patients with a phenotypic defect of a blood coagulation factor, especially von Willebrand factor (vWF); and
(ii) to extend the biological half-life of a protein in vivo (especially of factor VIII).
ADVANTAGE - In (A), (I) has increased biological half-life, i.e. the content and effect of endogenous or administered proteins are improved.
Dwg.0/2

L3 ANSWER 11 OF 14 BIOTECHNO COPYRIGHT 2004 Elsevier Science B.V. on STN

AN 1995:25266927 BIOTECHNO
TI Fibrinolysis inhibits shear stress-induced platelet aggregation
AU Kamat S.G.; Michelson A.D.; Benoit S.E.; Moake J.L.; Rajasekhar D.; Hellums J.D.; Kroll M.H.; Schafer A.I.
CS Medical Service, Houston VA Medical Center, 2002 Holcombe Blvd,Houston, TX 77030, United States.
SO Circulation, (1995), 92/6 (1399-1407)
CODEN: CIRCAZ ISSN: 0009-7322
DT Journal; Article
CY United States
LA English
SL English
AB Background: Shear stress-induced platelet aggregation may initiate arterial thrombosis at sites of pathological blood flow. Shear stress-induced platelet aggregation is mediated by von Willebrand factor (vWf) binding to platelet membrane glycoprotein (GP) Ib and GP IIb/IIIa. Tissue- type plasminogen activator (TPA) induces thrombolysis in coronary arteries through the local generation of plasmin. Plasmin also proteolyses GP Ib and plasma vWf. Methods and Results: Because these effects could mitigate shear stress-induced platelet aggregation, we investigated the effect of fibrinolytic agents on platelet aggregation in response to a pathological shear stress of 120 dynes/cm.sup.2 generated by a cone-and-platen rotational viscometer. Plasmin inhibited shear stress-induced aggregation of washed platelets, and this was associated with a decrease in GP Ib. TPA, at concentrations >= 2000 IU/mL, significantly inhibited shear stress-induced platelet aggregation of platelet-rich plasma without a decrease in platelet GP Ib. In plasma-platelet mixing experiments, we determined that the TPA effect was localized to plasma. Purified vWf multimer degradation by TPA (in the presence of exogenous plasminogen) was associated with the loss of the capacity of vWf to support shear stress-induced platelet aggregation. Conclusions: These results demonstrate that TPA inhibits platelet aggregation in response to pathological shear stress by altering the multimeric ***composition*** of vWf. This effect of TPA on shear stress-induced platelet aggregation may contribute, along with fibrinolysis, to the therapeutic effect of TPA in restoring blood flow during acute coronary artery thrombosis.

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